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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,939	04/11/2006	Christophe Revirron	05-403	8331

20306 7590 02/04/2009

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,939	REVIRRON, CHRISTOPHE	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 22-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10 and 22-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments, Rule 130, 131 and 132 affidavits and remarks received in the office on 11/19/2008. Claims 1-9, 11-21, 29 have been cancelled. Claims 10, 22-28 are pending and are being examined on the merits herein.

Response to Remarks

Applicants' arguments regarding the 103 rejections have been fully considered and found not to be persuasive. The rejections are maintained and are given below for Applicant's convenience. Accordingly, the office action is made Final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10, 22, 23, 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gensthaler (Pharmazeutische Zeitung, vol. 146, no. 7, 2001-02-15, p 35-36) in view of Scheinfeld (J of Drugs in Dermatology, Publication date 12/01/2002) and further in view of van Cauwenberge et al. (Applicants cited exhibit 4, Rule 132 declaration, 5/12/2008, Allergy, 2000, 55, 116-134).

Gensthaler teaches that Levocetirizine was effective in the treatment of patients with seasonal allergic rhinitis (p 35, para 4 lines 1-2). The reference further teaches an

intended study of the long-term effect of Levocetirizine in 500 adults with persistent allergic rhinitis (p 36, lines 3-8).

The reference does not teach a method of administration in a daily dosage of about 0.0005 mg to about 2 mg per kg of body weight in treating persistent allergic rhinitis patients or the number of dosages in the intended study of persistent allergic rhinitis.

Scheinfeld teach oral levocetirizine (5 mg once daily) for 32 days was reportedly effective in the treatment of patients with seasonal and perennial allergic rhinitis and further teach that levocetirizine relieves symptoms associated with house dust mite allergy (p 2, Heading: Uses to treat allergy, para 1, last line, para 2, lines 1-3). For example, administration of 5 mg of Levocetirizine to a 20 kg patient would amount to 0.25 mg/kg of body weight, or to a 40 kg patient would amount to 0.5 mg kg of body weight which falls within the range claimed in claims 22 and 23.

It would have been obvious to one of ordinary skill in the art to administer levocetirizine in the treatment of persistent allergic rhinitis because Gensthaler teaches the effectiveness of the compound in seasonal allergic rhinitis and further teaches the intended clinical study of persistent allergic rhinitis with the same compound. Hence one of ordinary skill in the art would have been motivated to administer levocetirizine in the treatment of persistent allergic rhinitis to obtain similar therapeutic benefits. It is known in the prior art that patients suffering from persistent allergic rhinitis are sensitive to indoor allergens like dust mites and perennial allergic rhinitis patients are sensitive to dust mites (J Allergy Clin Immunol. V 108, 5, S147, 2001). Hence one having ordinary

skill in the art would have been motivated to administer levocetirizine in the treatment of persistent allergic rhinitis because of expectation of success as Scheinfeld teach levocetirizine administration to subjects suffering from perennial rhinitis. As per Websters' dictionary (http://www.merriam-webster.com/dictionary/perennial) perennial is defined as 'present all seasons of the year' or 'persistent without interruption'. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention to have administered levocetirizine in a method of treatment of persistent allergic rhinitis. It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to administer a dose of 0.0005 mg to about 2 mg per kg of body weight per patient for the treatment of persistent allergic rhinitis because Scheinfeld teach levocetirizine administration of 5 mg dosage to subjects suffering from seasonal and perennial rhinitis. The references do not teach administration of split dosages (2-5) per day. One of ordinary skill in the art would have been motivated to adjust the dosage amount or dosages administered per day by routine experimentation as one can expect similar therapeutic benefits and safety in the administration of levocetirizine to patients with persistent allergy as Scheinfeld has shown the drug to be safe and therapeutically beneficial in the patients with seasonal and perennial allergy rhinitis. Optimization of the dose of the compound is not considered inventive because it is a matter of routine experimentation. Applicant's attention is directed to In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) which states, "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See MPEP § 2144.05, "11. Optimization of Ranges".

The references do not teach administration of levocetirizine for a period equal to more than 3 months.

van Cauwenberge et al. teach in a method of treatment of perennial allergic rhinitis that if the symptom control with antihistamines is inadequate or if the patient presents to the physician from the start with moderate to frequent symptoms a topical steroid is recommended for long term use up to several months (p 126, Heading: Perennial Allergic Rhinitis, para 4, lines 1-5).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have administered levocetirizine for a period equal to more than 3 months in a method of treatment of persistent allergic rhinitis because of van Cauwenberge et al.'s teachings. The reference teaches long term treatment (up to several months) of perennial allergic rhinitis in case the symptom control is inadequate with antihistamine or if the patients have moderate to frequent symptoms. One having ordinary skill in the art would have been motivated to administer levocetirizine for a period equal to more than 3 months in a method of treatment of persistent allergic rhinitis to alleviate all the symptoms of persistent allergic rhinitis if the symptoms persist longer than 3 months or if they are frequent and to effectively treat the disorder.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gensthaler (Pharmazeutische Zeitung, vol. 146, no. 7, 2001-02-15, p 35-36) in view of Scheinfeld (J of Drugs in Dermatology, Publication date 12/01/2002) and further in view of van Cauwenberge et al. (Applicants cited exhibit 4, Rule 132 declaration, 5/12/2008,

Allergy, 2000, 55, 116-134) as applied to claims 10, 22, 23, 25-28 above and further in view of Salmon et al. (US 2003/0236275).

Gensthaler, Scheinfeld and van Cauwenberge et al's teachings discussed as above.

The references do not teach administration of levocetirizine in administered via inhalation, topical etc. as claimed in claim 24.

Salmon et al. teaches antihistamines such as levocetirizine, desloratadine are useful in the treatment of seasonal allergic rhinitis. The reference teaches that antihistamines can be administered by different modes such as topical, inhalation, oral etc. (p 3, para 0037).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer levocetirizine by different routes of administration in a method of treatment for persistent allergic rhinitis because of the teachings of Salmun et al. Salmun et al teaches the administration of levocetirizine to be safe and beneficial in rhinitis patients and further teach that antihistamines can be administered by different modes such as topical, inhalation, oral etc. The different mode of administration is deemed obvious since it is within the knowledge of the skilled pharmacologist and represents conventional modes of administration.

Response to Arguments

Applicants' arguments and declaration by Dr. Bousquet have been fully considered and found not to be persuasive. Applicants' argue that previous and present office actions seem to assume that because SAR, PAR and PER all relate to allergic

rhinitis and people suffering from these afflictions frequently are sensitive to similar allergens (e.g., dust mites), those of ordinary skill in the art would have expected that treatments used for SAR and/or PAR would be equally applicable to PER as well, but the Office has provided no evidence of this. In response, the Gensthaler reference teaches that Levocetirizine was effective in the treatment of patients with seasonal allergic rhinitis. The reference further teaches an intended study of the long-term effect of Levocetirizine in 500 adults with persistent allergic rhinitis. It is evident from this reference alone for one of ordinary skill in the art that treatment of SAR could be applicable to persistent allergic rhinitis. The reference provides a suggestion to test levocetirizine, (the drug known to be useful for patients with SAR) in patients with persistent allergic rhinitis Thus from Gensthaler reference alone it would have been obvious to one of ordinary skill in the art at the time of the invention to try levocetirizine which has been shown in the prior art to be useful for the treatment of seasonal and perennial allergic rhinitis in a method of treatment of persistent allergic rhinitis. In addition, the newly classified intermittent and persistent allergies are classes of allergic rhinitis with overlapping symptoms with that of previously classified seasonal and perennial allergic rhinitis. For example, mite allergy is one of the symptoms (IDS document submitted: Bousquet, Clin Exp Allergy, 2005, 35, 728-32) in persistent and perennial allergic rhinitis. As stated in the previous office action argument, applicants' submitted IDS document (Medical and Other News (www.pslgroup.com/dg/207766.htm, doctor's guide, October 2001) teach in the references section, Potter et al, levocetirizine in the treatment of perennial allergic rhinitis in patients sensitized to house mite, Horak

et al. Effect of Levocetirizine and loratadine on symptom relief in house dust mite allergic patients exposed to allergen. The prior art document (IDS reference: J Allergy Clin Immunol. V 108, 5, S147, 2001) teach that majority of patients suffering from persistent allergic rhinitis are sensitized to mites (p S163, 3-1-3-1- Mites). The reference further teach that patients allergic to mites have symptoms all year around but with a recrudescence during the peak periods (p S163, 3-1-3-1- Mites) and the symptoms of patients allergic to mites are aggravated when it is humid. Hence there is clear evidence from the prior art teachings that mite allergy is a symptom of persistent, perennial and seasonal allergies. As stated above, in the rejection, Scheinfeld teaches that levocetirizine relieves symptoms associated with house dust mite allergy. Hence in addition to Gensthaler that provides suggestion that levocetirizine may be useful in treating persistent allergic rhinitis, the prior art references along with Scheinfeld clearly indicates mite allergy as a common symptom between the newly classified and previously classified allergic rhinitis. Thus it is evident from the teachings of the prior art that one having ordinary skill in the art would have tried using levocetirizine in treating persistent allergic rhinitis and would have expected success in treating mite allergy symptoms.

Applicants argue that the Rule 132 Declaration submitted by the applicants provides evidence and establishes that ordinary skill in the art would not and could not have reasonably extrapolated the results observed with SAR and/or PAR to PER. In response, the examiner acknowledges the fact that intermittent and persistent allergic rhinitis is classified differently from the previously classified seasonal and perennial

allergic rhinitis. The primary reference used in the rejection, namely Gensthaler teaches an intended study of the long-term effect of Levocetirizine in 500 adults with persistent allergic rhinitis (p 36, lines 3-8). Hence it would have been obvious to one of ordinary skill in the art at the time of the invention to try levocetirizine in a method of treating persistent allergic rhinitis from the studies of Gensthaler alone. In addition, the secondary reference has been used to show the safe amounts of dosages of levocetirizine that can be administered to the patients. Mite allergy has been found to be a common symptom between persistent and seasonal allergic rhinitis (as evidenced above). Scheinfeld teaches that levocetirizine relieves symptoms associated with house dust mite allergy. Thus it is evident from the teachings of the prior art that one having ordinary skill in the art would have tried using levocetirizine in treating persistent allergic rhinitis and would have expected success in treating mite allergy symptoms.

Applicants' further argue that the Office has not addressed the Rule 132 Declaration. In response, the office has fully considered the declaration. The declaration by Dr. Bousquet discusses in detail the different allergic conditions and how they differ and newly classified intermittent and persistent allergic rhinitis cannot be used interchangeably and why it would have not been predictable to treat PER with levocetirizine based on the teachings of Gensthaler in view of Leynadier or Salmun. The examiner acknowledges the fact that PER is differently classified than SAR or PAR. However, the intermittent and persistent allergic rhinitis (according to the new definitions) has overlapping symptoms. Furthermore, Gensthaler teachings indicate an intended study of the long-term effect of Levocetirizine in 500 adults with persistent

allergic rhinitis. Thus this reference provides a suggestion to one of ordinary skill in the art to try using levocetirizine in a method of treating persistent allergic rhinitis. The secondary reference, Scheinfeld is cited to show the administration and dosages of the drug, levocetirizine. Moreover from Gensthaler's teachings and from the prior art teachings indicated above in the arguments section there are symptoms that overlap with the newly classified and the old SAR and PAR and one such is mite allergy. The prior art document (IDS reference: J Allergy Clin Immunol. V 108, 5, S147, 2001) teach that majority of patients suffering from **persistent** allergic rhinitis are sensitized to mites (p S163, 3-1-3-1- Mites). Applicants' submitted IDS document (Medical and Other News (www.pslgroup.com/dg/207766.htm, doctor's guide, October 2001) teach in the references section, Potter et al, levocetirizine in the treatment of perennial allergic rhinitis in patients sensitized to house mite, Horak et al. Effect of Levocetirizine and loratadine on symptom relief in house dust mite allergic patients exposed to allergen. Hence there is clear evidence from the prior art teachings that mite allergy is a symptom of persistent, perennial and seasonal allergies. In addition, the workshop conducted by Dr. Bousquet in Oct 2002, (prior to the instant invention) lists the symptoms sneezing, rhinorrhea, nasal congestion, nasal obstruction, conjunctivitis as symptoms suggestive of allergic rhinitis for the newly classified intermittent or persistent rhinitis that is common with some of the symptoms of SAR such as sneezing, rhinorrhea, nasal congestion, nasal pruritus, ocular pruritis (Leynadier et al. Acta Otorhinolaryngol Belg. 2001, 55(4): 305-12). It would have been obvious to one having ordinary skill in the art

at the time of the invention to try to use levocetirizine in the treatment of PER because of the common symptoms between SAR and PER in addition to Gensthaler's teachings.

Applicants' argue that the Office's reliance on the dictionary definition of "perennial" is contrary to established law. In response, the office does not use the definition to imply that perennial and persistent allergic rhinitis are the same. The office acknowledges the fact that PER is differently classified than SAR or PAR. The definition has been used to show that it would have been obvious to one of ordinary skill in the art at the time of the invention to try levocetirizine shown to be useful for the treatment of perennial and seasonal allergic rhinitis in the treatment of persistent allergic rhinitis.

Applicants' argue that it is plainly not obvious from van Cauwenberge et al. studies to use an antihistamine for an extended period. In response, the reference has been cited to show that drugs can be used in an extended period for up to several if the allergy symptoms persist.

Conclusion

No claims are allowed.

The rejections from the previous office action are maintained. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617